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EXAMINER	
STITZEL, DAVID PAUL	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/807,828	HILDEBRAND ET AL.	
	Examiner	Art Unit	
	David P. Stitzel, Esq.	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 51* is/are pending in the application.

4a) Of the above claim(s) *28-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-27 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

OFFICIAL ACTION

Restriction/Election

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-27 and 51 are drawn to a system for delivering to cerebrospinal fluid an injectable pharmaceutical composition in a therapeutically effective amount sufficient to treat pain.

II. Claims 28-50 are drawn to a method of treating pain by administering a therapeutically effective amount of an injectable pharmaceutical composition to cerebrospinal fluid via a system.

Inventions I and II are related as a product and a method of using said product. The inventions can be shown to be distinct if either or both of the following can be shown that: (1) the method of using the product as claimed can be practiced with another materially different product; or (2) the product as claimed can be used by another method that is materially different from the instantly claimed method of using said product (MPEP § 806.05(f)). In the instant case, the system as claimed in Invention I can be used by another method that is materially different from the method claimed in Invention II. For example, as opposed to using said system for delivering to cerebrospinal fluid an injectable pharmaceutical composition comprising gabapentin in a therapeutically effective amount sufficient to treat pain, said system may alternatively be used for delivering to cerebrospinal fluid an injectable pharmaceutical composition comprising gabapentin in a therapeutically effective amount sufficient to treat epilepsy.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Conclusion to Restriction Requirement

The Examiner has required restriction between product and methods of making claims. Where Applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn methods of making claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Methods of making claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. If claims are added after the election, Applicants must explicitly indicate which claims are readable upon the elected species. See MPEP § 809.02(a). Amendments submitted after final rejection are governed by 37 CFR 1.116. Amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined methods of making claims will be withdrawn, and the rejoined methods of making claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. §§ 101, 102, 103 and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and methods of making claims may be maintained. Withdrawn methods of making claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the methods of making claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include

the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. § 121 does not apply where the restriction requirement is withdrawn by the Examiner before the patent issues. See MPEP § 804.01.

Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named Inventors is no longer an actual Inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

During a telephone conversation with Mr. Keith M. Campbell, Esq. on Tuesday, November 16, 2005, at approximately 5:15 P.M., a provisional election was made *without traverse* to prosecute the Invention of Group I, claims 1-27 and 51. As a result and pursuant to 37 CFR § 1.142(b), claims 29-57 are withdrawn from further consideration as being drawn to a non-elected invention.

Status of Claims

As previously discussed, claims 28-50 are withdrawn from further consideration as being drawn to a non-elected invention. On the other hand, claims 1-27 and 51 are drawn to the elected Invention of Group I. As a result, claims 1-27 and 51 are currently pending and therefore examined herein on the merits for patentability.

Provisional Nonstatutory Double Patenting

A nonstatutory double patenting rejection of the "obviousness-type" is based on a judicially created doctrine grounded in public policy so as to prevent not only the unjustified or improper timewise extension of the "right to exclude" granted by a patent, but also possible harassment by multiple

assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re White*, 405 F.2d 904, 160 USPQ 417 (CCPA 1969); *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968); and *In re Sarett*, 327 F.2d 1005, 140 USPQ 474 (CCPA 1964).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned or assigned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. See MPEP § 804. However, this does not mean that one is absolutely precluded from all use of the patent disclosure. See MPEP § 804. For example, the specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Furthermore, ***those portions of the specification which provide support for the patent claims may also be examined and considered*** when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-442, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* stated that one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court in *Vogel* also pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior

art, nor is it applying the patent as a reference under 35 U.S.C. § 103, since only the disclosure of the invention claimed in the patent may be examined."

1. Claims 1-23, 25-27 and 51 of the instant application (10/807828) are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-28 and 58-59 of copending U.S. Patent Application Serial Number 10/807827 (hereinafter the conflicting Hildebrand '827 application).

More specifically, claims 1-23, 25-27 and 51 of the instant application are directed to a system comprising a pump, which is coupled to a reservoir and a catheter, for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: baclofen; and a GABA agonist (i.e., valproic acid or sodium valproate); wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Claims 1-28 and 58-59 of the conflicting Hildebrand '827 application are directed to a system comprising a pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: baclofen and sodium valproate; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said baclofen is present in said aqueous saline

solution at a concentration from about 50 μg/mL to about 3000 μg/mL; wherein said sodium valproate is present in said aqueous saline solution at a concentration from about 1 mg/mL to about 100 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

In conclusion, although claims 1-23, 25-27 and 51 of the instant application are not identical to claims 1-28 and 58-59 of the conflicting Hildebrand '827 application, the aforementioned claims are not patentably distinct each from the other because not only are all of the aforementioned claims substantially overlapping in scope, but also claims 1-23 are generic to all of the limitations recited in claims 1-18 of the conflicting Hildebrand '827 application.

2. Claims 1-27 and 51 of the instant application 10/807828 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-45 and 51 of copending U.S. Patent Application Serial Number (10/808129) (hereinafter the conflicting Hildebrand '129 application).

More specifically, claims 1-27 and 51 of the instant application are directed to a system comprising an external or implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: an opioid agonist; baclofen; and a GABA agonist (i.e., valproic acid or sodium valproate); wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said

aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Claims 1-45 and 51 of the conflicting Hildebrand '129 application are directed to a heat sterilized injectable pharmaceutical composition comprising an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: baclofen, morphine and hydromorphone; wherein said morphine may be present at a concentration from about 10 mg/mL to about 50 mg/mL; wherein said hydromorphone may be present at a concentration from about 1 mg/mL to about 20 mg/mL; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers; wherein said heat sterilized injectable pharmaceutical composition is packaged within a kit that further comprises instructions.

Although the aforementioned claims of the conflicting Hildebrand '129 application do not explicitly recite the instantly claimed system comprising an implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to utilize a system comprising an implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, as the conflicting Hildebrand '129 application explicitly teaches utilizing a system comprising an implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid ([0043]-[0048]). Therefore, one of ordinary skill in

the art would have been motivated to utilize a system comprising an implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid.

In conclusion, although claims 1-27 and 51 of the instant application are not identical to claims 1-45 and 51 of the conflicting Hildebrand '129 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope.

3. Claims 1-27 and 51 of the instant application 10/807828 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over conflicting claims 1-48 of copending U.S. Patent Application Serial Number 10/808054 (hereinafter the conflicting Hildebrand '054 application).

More specifically, claims 1-27 and 51 of the instant application are directed to a system comprising an external or implantable pump for intrathecal administration of an injectable pharmaceutical composition into cerebrospinal fluid, wherein said injectable pharmaceutical composition comprises an aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: an opioid agonist; baclofen; and a GABA agonist (i.e., valproic acid or sodium valproate); wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity that is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

Claims 1-48 of the conflicting Hildebrand '054 application are directed to a system comprising an implantable pump for intrathecal administration of a heat sterilized injectable pharmaceutical composition into cerebrospinal fluid, wherein said heat sterilized injectable pharmaceutical composition comprises an

aqueous saline solution of gabapentin in combination with an additional therapeutic agent selected from the following: sodium valproate, midazolam, baclofen, morphine and hydromorphone; wherein said morphine may be present at a concentration from about 10 mg/mL to about 50 mg/mL; wherein said hydromorphone may be present at a concentration from about 1 mg/mL to about 20 mg/mL; wherein said gabapentin is present in said aqueous saline solution at a concentration of greater than about 30 mg/mL; wherein said aqueous saline solution has a pH between about 4 and about 9; wherein said aqueous saline solution has a tonicity of about 250 mOsm, which is substantially isotonic with cerebrospinal fluid; wherein said aqueous saline solution is substantially free of preservatives and buffers.

In conclusion, although claims 1-27 and 51 of the instant application are not identical to claims 1-48 of the conflicting Hildebrand '054 application, the aforementioned claims are not patentably distinct each from the other because said claims are substantially overlapping in scope.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraph of 35 U.S.C. § 103, which forms the basis of the obviousness rejections as set forth under this particular section of the Official Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-19, 22-27 and 51 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pre-Grant Patent Application Publication Number 2001/0036943 (hereinafter the Coe '943 publication) in view of U.S. Patent 6,495,601 (hereinafter the Hochman '601 patent).

With respect to claims 1-19, 22-27 and 51 of the instant application, the Coe '943 publication teaches a injectable pharmaceutical composition ([0004], [0283] and [0370]), which may comprise: an anticonvulsant analgesic, such as gabapentin and valproic acid ([0006], [0138] and [0270]); a non-opioid analgesic, such as baclofen ([0004], [0006] and [0270]); an opioid analgesic, such as morphine and hydromorphone (a.k.a., Dilaudid) ([0004], [0006], [0138] and [0270]); and a pharmaceutically acceptable carrier ([0004], [0006], [0368] and [0369]). Gabapentin may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 10.0 mg/kg/day to 35.0 mg/kg/day ([0315]). Valproic acid may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 1.0 mg/kg/day to 60.0 mg/kg/day ([0319]). Baclofen may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.1 mg/kg/day to 0.5 mg/kg/day ([0315]). The pharmaceutically acceptable carrier is an aqueous isotonic saline solution ([0370]). Morphine may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.1 mg/kg/day to 4.0 mg/kg/day ([0303]). Hydromorphone may be present in an amount from 0.1% by weight to 95% by weight of said pharmaceutical composition ([0373]) and parenterally administered ([0283] and [0370]) in an amount from 0.01 mg/kg/day to 2.0 mg/kg/day ([0301]). The pharmaceutically acceptable carrier is a sterile aqueous isotonic saline solution ([0370]). The pharmaceutically acceptable carrier is a sterile aqueous isotonic saline solution ([0370]). In regard to claims 18-19 and 21 in particular, the Coe '943 publication is utterly devoid of any teachings of the utilization of preservatives and merely mentions that said sterile aqueous isotonic saline solution may be

suitably buffered, if necessary, so as to render said injectable pharmaceutical composition possessing an osmolality suitable for parenteral administration.

While the Coe '943 publication does not explicitly teach a system comprising an implantable pump, which is coupled to a reservoir and a catheter, and a patient controlled activator for intrathecal or epidural administration of an injectable pharmaceutical composition into cerebrospinal fluid, the Coe '943 publication does in fact teach parenteral administration of said injectable pharmaceutical composition ([0283] and [0370]). However, the Hochman '601 patent teaches intrathecal or epidural administration (column 12, lines 60-67; and column 14, lines 9-12) via a system comprising an implantable pump (column 7, lines 40-44; column 13, lines 23-33, 38-39 and 49-53; column 14, lines 51-52) for delivering to cerebrospinal fluid via intrathecal or epidural administration (column 12, lines 60-67; column 13, lines 31-33; and column 14, lines 9-12), an injectable pharmaceutical composition comprising gabapentin and valproate (column 14, lines 42-67; and column 15, lines 1-47) in a therapeutically effective amount sufficient to treat pain (column 6, lines 22-25; column 13, lines 58-60; column 14, lines 45-46 and 50; and column 15, lines 39-43). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to administer said injectable pharmaceutical composition intrathecally or epidurally via a system comprising an implantable osmotic pump, which is coupled to a reservoir and a catheter, and a patient controlled activator, as parenteral administration by definition includes any route of administration (i.e., intrathecal or epidural) other than enteral (i.e., oral) administration. In addition, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to not only couple a therapeutic agent containing reservoir to said implantable pump, but also couple a catheter to said implantable pump so as to provide a means for delivering said injectable pharmaceutical composition to cerebrospinal fluid by intrathecal or epidural

administration via said system equipped with a patient controlled activator. Furthermore, it would have also been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to incorporate the injectable pharmaceutical composition, of the Coe '943 publication, into a system comprising an implantable pump having a therapeutic agent containing reservoir, a catheter coupled to said implantable osmotic pump, and a patient controlled activator so as to provide a means for delivering said injectable pharmaceutical composition to cerebrospinal fluid by intrathecal or epidural administration via said system. Therefore, one of ordinary skill in the art would have been motivated to incorporate said injectable pharmaceutical composition comprising gabapentin, a GABA agonist (i.e., valproic acid and sodium valproate), baclofen and/or an opioid agonist (i.e., morphine and hydromorphone) into said therapeutic agent containing reservoir, which is coupled to said implantable osmotic pump, so as to provide for a system of said injectable pharmaceutical composition, as suggested by the Hochman '601 patent.

With respect to claims 24-26 of the instant application, although the Coe '943 publication does not explicitly teach the instantly claimed combination, the Coe '943 publication does teach that said sterile injectable pharmaceutical composition may comprise an anticonvulsant analgesic in combination with a non-opioid and/or opioid analgesic for the treatment of pain ([0006], [0138], [0270], [0368] and [0373]). More specifically, the Coe '943 publication teaches that gabapentin, valproic acid, baclofen, morphine and hydromorphone are particularly useful in the treatment of pain ([0006], [0138], [0270], [0368] and [0373]). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to in fact utilize gabapentin in combination with valproic acid, baclofen, morphine and/or hydromorphone. One of ordinary skill in the art would have been motivated to combine gabapentin together with valproic acid, baclofen, morphine and/or hydromorphone within said sterile

injectable pharmaceutical composition, so as to obtain a sterile injectable pharmaceutical composition that is particularly useful in the treatment pain, as suggested by the Coe '943 publication. In addition, although the Coe '943 publication teaches utilizing valproic acid as an anticonvulsant analgesic, the Coe '943 publication does not explicitly teach utilizing the sodium salt of valproic acid, namely sodium valproate (a.k.a., valproate). However, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to utilize valproate, as valproate is merely the sodium salt of valproic acid, as one of ordinary skill in the art would reasonably expect that the sodium salt of valproic acid would also exhibit anticonvulsant analgesic activity similar, if not identical, to that of valproic acid. Furthermore, while the Coe '943 publication does not explicitly teach utilizing valproate in combination with gabapentin, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the injectable pharmaceutical composition of the Coe '943 publication to utilize gabapentin in combination with valproate, as the Hochman '601 patent explicitly teaches utilizing not only gabapentin, but also valproate in the treatment of pain associated with migraine headaches (column 3, lines 19-24; column 6, lines 20-43; column 8, lines 31-42; column 14, lines 42-67; and column 15, lines 1-47). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to utilize gabapentin in combination with valproic acid, sodium valproate, baclofen, morphine and/or hydromorphone within said injectable pharmaceutical composition so as to impart desired analgesic properties to said injectable pharmaceutical composition. One of ordinary skill in the art would have been motivated to utilize gabapentin in combination with a GABA agonist (i.e., valproic acid and sodium valproate), baclofen and/or an opioid agonist (i.e., morphine and hydromorphone) within said injectable pharmaceutical composition so as to

obtain an injectable pharmaceutical composition, which is particularly useful in the treatment pain, as suggested by the Hochman '601 patent.

With respect to claims 11-14 of the instant application, although the Coe '943 publication explicitly teaches that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution for parenteral administration ([0283], [0368], [0370] and [0372]), the Coe '943 publication does not explicitly teach a specific numerical value of osmolality that is isotonic with cerebrospinal fluid, wherein said sterile injectable pharmaceutical composition further comprises less than 0.9% weight per volume of sodium chloride. However, parenteral administration by definition includes any route of administration (i.e., intrathecal or epidural) other than enteral (i.e., oral) administration. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to utilize an appropriate weight per volume of sodium chloride so as to render an sterile injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired osmolality that is isotonic with cerebrospinal fluid thereby rendering said sterile injectable pharmaceutical composition suitable for parenteral administration via intrathecal or epidural injection.

With respect to claims 15-17 and 21 of the instant application, although the Coe '943 publication does not explicitly teach a specific pH that is physiologically similar to that of cerebrospinal fluid, the Coe '943 publication does teach that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution, which is suitably buffered, if necessary, for parenteral administration and is readily obtainable by standard techniques well known to those of ordinary skill in the art ([0283], [0368], [0370] and [0372]). Parenteral administration by definition includes any route of administration (i.e., intrathecal or epidural) other than enteral (i.e., oral) administration. Therefore, it would have been

prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to utilize a pH buffer, if necessary, so as to render an injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired pH suitable for parenteral administration so as to render an sterile injectable pharmaceutical composition comprising a sterile aqueous isotonic saline solution possessing a desired pH that is physiologically similar to that of cerebrospinal fluid thereby rendering said sterile injectable pharmaceutical composition suitable for parenteral administration via intrathecal or epidural injection.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element as recited in the aforementioned claims, as a whole, would have been reasonably suggested by the teachings of the cited prior art references.

2. Claims 11-17 and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pre-Grant Patent Application Publication Number 2001/0036943 (hereinafter the Coe '943 publication) in view of U.S. Patent 6,495,601 (hereinafter the Hochman '601 patent) and in further view of U.S. Patent 4,755,388 (hereinafter the Heath '388 patent).

The teachings of the Coe '943 publication in view of the Hochman '601 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 11-14 of the instant application, although the Coe '943 publication explicitly teaches that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution for parenteral administration ([0283], [0368], [0370] and [0372]), the Coe '943 publication does not explicitly teach a specific numerical value of osmolality that is isotonic with

cerebrospinal fluid, wherein said sterile injectable pharmaceutical composition further comprises less than 0.9% weight per volume of sodium chloride. However, the Heath '388 patent teaches an aqueous gabapentin drug composition comprising an osmotic modifier, such as an aqueous saline solution (column 3, lines 10-20; and column 5, lines 6-9), whereby said aqueous gabapentin drug composition can be formulated in a manner such that said aqueous gabapentin drug composition has an osmolality from about 250 mOsm/kg to about 350 mOsm/kg, thereby rendering said aqueous gabapentin drug composition isotonic with physiological cerebrospinal fluid. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the injectable pharmaceutical composition of the Coe '943 publication by incorporating an appropriate weight per volume of sodium chloride (i.e., less than or equal to 0.9% weight per volume of sodium chloride) thereby rendering said aqueous gabapentin drug composition having a specific osmolality from about 250 mOsm/kg to about 350 mOsm/kg, which is isotonic with cerebrospinal fluid, as suggested by the Heath '388 patent, so as to provide for parenteral administration of said injectable pharmaceutical composition via intrathecal or epidural administration.

With respect to claims 15-17 and 21 of the instant application, although the Coe '943 publication explicitly teaches that said sterile injectable pharmaceutical composition comprises a sterile aqueous isotonic saline solution, which is suitably buffered, if necessary, for parenteral administration ([0283], [0368], [0370] and [0372]), the Coe '943 publication does not explicitly teach a specific pH that is physiologically similar to that of cerebrospinal fluid. However, the Heath '388 patent teaches an aqueous gabapentin drug composition comprising a pH buffer (column 3, lines 10-20; and column 5, lines 6-9), whereby said aqueous gabapentin drug composition can be formulated in a manner such that said aqueous gabapentin drug composition has a pH from about 6 to about 9, thereby rendering said aqueous

gabapentin drug composition having a pH that is physiologically similar to that of cerebrospinal fluid. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the injectable pharmaceutical composition of the Coe '943 with a pH buffer, if necessary, so as to impart not only a specific pH from about 6 to about 9, preferably from about 6 to about 8, and more preferably from about 6.5 to about 7.5, which is physiologically similar to that of cerebrospinal fluid, as suggested by the Heath '388 patent, so as to provide for parenteral administration of said injectable pharmaceutical composition via intrathecal or epidural administration.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element as recited in the aforementioned claims, as a whole, would have been reasonably suggested by the teachings of the cited prior art references.

3. Claims 20-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Coe '943 publication in view of the Hochman '601 patent, and in further view of U.S. Patent 6,054,482 (hereinafter the Augart '482 patent).

The teachings of the Coe '943 publication in view of the Hochman '601 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 20-21 of the instant application, while neither the Coe '943 publication, nor the Hochman '601 patent teach a specific weight per volume percentage of the corresponding undesirable lactam within said composition, the Augart '482 patent teaches a pharmaceutical composition comprising gabapentin, wherein the specific weight percent of the corresponding undesirable lactam within said composition is less than or equal to 0.5% by weight (abstract; column 1, lines 10-21; column 2, lines 16-

52; column 3, lines 26-35; column 4, lines 50-53; column 5, lines 5-67; and column 6, lines 1-5). It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the Coe '943 publication in view of the Hochman '601 patent with the teachings of the Augart '482 patent, so as to provide a pharmaceutical composition comprising gabapentin, wherein said composition has a weight percent of the corresponding undesirable lactam of less than or equal to 0.5% by weight. One of ordinary skill in the art would have been motivated to decrease the concentration of the corresponding undesirable lactam so as to thereby decrease the level of toxicity within said composition, said toxicity being associated with and attributable to the amount of corresponding undesirable lactam present with said composition, as taught by the Augart '482 patent (column 4, lines 50-53).

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element as recited in the aforementioned claims, as a whole, would have been reasonably suggested by the teachings of the cited prior art references.

4. Claims 20-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Coe '943 publication in view of the Hochman '601 patent, and in further view of U.S. Pre-Grant Patent Application Publication Number 2002/0198261 (hereinafter the Kulkarni '261 publication).

The teachings of the Coe '943 publication in view of the Hochman '601 patent are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

With respect to claims 1, 3-6 and 20-21 of the instant application, while neither the Coe '943 publication, nor the Hochman '601 patent teach a specific weight per volume percentage of the

corresponding undesirable lactam within said composition, the Kulkarni '261 publication teaches a pharmaceutical composition comprising gabapentin, wherein the specific weight percent of the corresponding undesirable lactam within said composition is less than or equal to 0.5% by weight (abstract; [0001]-[0007]; [0009]-[0015]; [0068]; [0071]-[0072]; [0074]; [0077]; [0080]-[0085]; and claim 14). It would have been prima facie obvious to one of ordinary skill in the art at the time the instant application was filed to modify the Coe '943 publication in view of the Hochman '601 patent with the teachings of the Kulkarni '261 publication, so as to provide a pharmaceutical composition comprising gabapentin, wherein said composition has a weight percent of the corresponding undesirable lactam of less than or equal to 0.5% by weight. One of ordinary skill in the art would have been motivated to decrease the concentration of the corresponding undesirable lactam so as to thereby decrease the level of toxicity within said composition, said toxicity being associated with and attributable to the amount of corresponding undesirable lactam present with said composition, as taught by the Kulkarni '261 publication [0010] and [0077].

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because each and every element as recited in the aforementioned claims, as a whole, would have been reasonably suggested by the teachings of the cited prior art references.

Conclusion

Claims 28-50 were withdrawn from consideration as being drawn to a non-elected invention. Claims 1-27 and 51 are rejected.

Contact Information

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to David P. Stitzel, Esq. whose telephone number is 571-272-8508. The Examiner can normally be reached on Monday-Friday, from 7:30AM-6:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Sreenivasan Padmanabhan can be reached at 571-272-0629. The central fax number for the USPTO is 571-273-8300.

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